How to Identify White Coat Hypertension at The First Diagnosis: Establishment of A Scoring Model for The Differential Diagnosis of White Coat Hypertension and Sustained Hypertension

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Research

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Abstract

Background: To establish a scoring model for the differential diagnosis of white coat hypertension (WCH) and sustained hypertension (SHT).

Methods: 553 adults with elevated office blood pressure, normal renal function and no antihypertensive drugs were included in this study. 17 parameters, such as gender and age, were obtained by questionnaire investigation and biochemical index detection. WCH and SHT were distinguished by 24-hour ambulatory blood pressure monitoring. Participants were randomly divided into a training set (445 cases) and a verification set (108 cases). In the training set, the above parameters were screened by LASSO regression and univariate logistic regression analysis, then, the scoring model was constructed through multivariate logistic regression analysis. ROC curve and calibration curve were used to discuss the discrimination and calibration of this scoring model respectively

Results: 6 parameters were finally selected, namely isolated systolic hypertension, systolic blood pressure, diastolic blood pressure, triglyceride, serum creatinine, and cardiovascular and cerebrovascular diseases. Multivariate logistic regression was used to establish the scoring model. The R^2 and AUC of the scoring model in the training set were 0.163 and 0.705, respectively. In the verification set, the R^2 of the scoring model was 0.206, and AUC was 0.718. The calibration test results showed that the scoring model had good stability in both training set and verification set (MSE=0. 001, MAE=0. 014; MSE=0. 001, MAE=0. 025, respectively).

Conclusion: A stable scoring model for distinguishing WCH can be established, which can assist clinical medical workers to identify WCH at the first diagnosis.

Background

In the clinical practice, the differential diagnosis of white coat hypertension (WCH) and sustained hypertension (SHT) is of great significance. Both WCH and SHT are highly prevalent diseases, but the target organ damage effects of WCH and SHT are far from each other [1, 2]. SHT is a hypertension subtype with definite damage to various target organs [3]. However, whether WCH is only a benign clinical phenomenon or a criminal clinical disease is still controversial [4]. Especially since the European society of hypertension practice guidelines (2014 edition) revised the diagnostic criteria for WCH and excluded isolated nocturnal hypertension with definite target organ injury effect from WCH, the definite cardiovascular and cerebrovascular injury effect of WCH has not been found in many clinical studies [5, 6]. For example, a large-scale clinical study including 115,708 samples in 2017 did not find cardiovascular injury of WCH with normal ambulatory blood pressure in each time period [7]. Both WCH and SHT showed elevated office blood pressure, but the effects of cardiovascular and cerebrovascular injury were significantly different [8]. Reasonable discrimination between WCH and SHT in the clinical practice is helpful for medical personnel to understand the blood pressure status of patients more comprehensively and provide more reasonable treatment schemes.

Although the clinical identification of WCH and SHT is so important, the initial identification of WCH and SHT has always been a difficult problem in the clinical practice [9]. At present, the identified methods include home blood pressure measurement and ambulatory blood pressure monitoring [10, 11]. At present, home self-test blood pressure is not popular, the method of measuring home blood pressure for the general population is not standardized, and home self-test blood pressure cannot reflect the night blood pressure level, and its differential effect between WCH and SHT is lower than ambulatory blood pressure monitoring [12]. However, the clinical application of 24-hour ambulatory blood pressure monitoring also requires newly diagnosed patients to spend more time and cost, especially it takes more than 24 hours to identify WCH and SHT when returning to the clinic, which is unacceptable to some patients. If medical personnel can predict the WCH risk of patients with increased office blood pressure during the initial diagnosis, ambulatory blood pressure monitoring can be selectively carried out, and clinical treatment can be carried out more reasonably.

Some medical workers empirically distinguish patients with elevated office blood pressure in clinical practice to judge whether WCH exists. Of course, this is based on the fact that clinicians have a certain understanding of the clinical characteristics of WCH and SHT. Previous literature reports suggest that WCH is often high in women, and clinically characterized by isolated systolic hypertension (ISH), but the incidence rate of WCH is low among smokers, while SHT shows more obvious blood lipid and renal function abnormalities, and is more prone to cardiovascular and cerebrovascular diseases [13-15]. Some medical personnel make an empirical evaluation of WCH and SHT based on known clinical characteristics, but there is a lack of a scientific quantitative scoring method. The gradual application of the scoring model for differential diagnosis in recent years has provided it with the possibility. The scoring model belongs to the risk prediction models. Its outstanding advantage is that it can combine several differential variables through the regression equation to improve the identification ability, and it can vividly measure the disease risk by drawing nomogram [16, 17]. The purpose of this study is to construct a scoring model for differential diagnosis of WCH and SHT through the least absolute shrinkage and selection operator (LASSO) regression, univariate and multivariate logistic regression analysis and other statistical methods, and hope to apply it to clinical practice.

Methods

Study participants

Between April 2018 and June 2020, 826 adults with elevated office blood pressure were recruited as participants in Daping Hospital. Participants were further screened through the following two exclusion criteria: (1) antihypertensive drug users; (2) renal insufficiency (Scr ≥ 133 mol/L) [18]. The study was reviewed and approved by the Ethics Committee of Daping Hospital of the Army Medical University and registered in the Chinese Clinical Trial Registry with the registration number ChiCTR1800015507. All participants gave informed consent to the study.

General clinical Information

The age, sex, smoking history, drinking history, diabetes history, and cardiovascular and cerebrovascular disease history of the participants were collected through questionnaires. The height and weight of the selected participants were measured, and the body mass index (BMI) was calculated. The calculation formula was (BMI) = weight (kg) ÷ height ^{2} (m) [19]

Blood pressure measurement

After the participants took a seat rest in the clinic for 20 minutes, the blood pressure of the right brachial artery was measured 3 times by professional medical personnel with mercury sphygmomanometer. The average value of blood pressure measurement was taken as office blood pressure measurement result [20].

24-hour ambulatory blood pressure monitoring was carried out by ambulatory ECG blood pressure recorder CB-2301-A (Wuxi, China), with 6: 00-22: 00 as daytime blood pressure and 22: 00-6: 00 as nighttime blood pressure. Daytime blood pressure measurement is conducted every 30 minutes, the number of effective sphygmomanometers should be above 80%, and nighttime blood pressure requires effective blood pressure every hour.

WCH and SHT were distinguished according to office blood pressure and 24-hour ambulatory blood pressure. European Hypertension Practice Guideline Standard (2014 Edition) was adopted, and the blood pressure rise boundary point was set at office blood pressure ≥ 140/90 mmHg. The average ambulatory blood pressure was ≥ 135/85 mmHg during the daytime, ≥ 120/70 mmHg during the nighttime, and ≥ 130/80 mmHg during the whole day [21, 22]. SHT was defined as elevated office blood pressure and ambulatory blood pressure. While, WCH only showed elevated office blood pressure [23].

Biochemical detection

The total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (Glu), serum creatinine (Scr) and uric acid (UA) were measured by BECKMAN AU5800 biochemical analyzer. Diabetes mellitus (DM) is defined as the previous definite diagnosis of diabetes mellitus, or the fasting blood glucose detected this time is ≥ 7.0 mmol/L [24].

Division of training set and verification set

Using RStudio software (Version 1.3. 959), the participants were divided into the training set and the verification set, and the ratio of training set to verification set was 4:1. The statistical differences of age, sex, WCH prevalence rate, and other research variables between the training set and the verification set were compared. The differences of research variables between WCH patients and SHT patients in training set and verification set were also analyzed respectively. The counting data is expressed as the number of cases (%), and the Pearson chi-square test is used for statistical analysis. The measurement data are

expressed as median (IQR, interquartile range), and the statistical analysis method adopts Kruskal-Wallis rank-sum test [25, 26]. The above statistical analysis was performed by SPSS (Version 22.0) software.

Model construction

LASSO regression and univariate logistic regression were used to select the variables of the model. The study variables involved in the screening process included sex, age, body mass index (BMI), smoking history, drinking history, isolated systolic hypertension (ISH), systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), diabetes mellitus (DM), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), creatinine (Scr), uric acid (UA) and cardiovascular and cerebrovascular diseases (CCVD). Firstly, the least absolute shrinkage and selection operator (LASSO) regression model was constructed in the training set. LASSO regression algorithm, which is suitable for the regression of high-dimensional data and interactive data analysis, was conducted by 10-fold cross-validation with penalty parameter tuning based on minimum criteria and 1 standard error of the minimum criteria (the 1-SE criteria) in the training set. Since increasing the number of independent variables of the model cannot significantly improve the performance of the model after the value reaches a certain value, the 1-SE criteria can give the model with excellent performance but the least number of independent variables, so we generally adopt this criteria [27]. We further carried out univariate logistic regression analysis on the research variables corresponding to the 1-SE criteria, and included the research variables with statistical differences as the final model construction variables. Multivariate logistic regression analysis was used to construct the scoring model of WCH, and the corresponding nomogram was drawn [28]. The R language packets used mainly include "readxl", "glmnet", "informationValue", "rms", "pROC" and so on.

Discrimination test

Firstly, the receiver operating curve (ROC) was used in the training set to test the discrimination degree of the scoring model in the training set, and the coefficient of determination (R^2), the area under the ROC curve (AUC) and its 95% confidence interval (95% CI) are obtained. Furthermore, after applying the scoring model to the verification set, the ROC curve was used to evaluate the discrimination degree of the verification set model, and whether the discrimination degree was similar to the training set model was observed [29].

Calibration degree test

Firstly, the Bootstrap method was used to randomly select samples 1000 times in the training set to verify the calibration degree of the model. The corresponding Calibration curves are made, and the mean square error (MSE) and mean absolute error (MAE) values are calculated to evaluate the model. The lower the MAE and MSE, the better the stability of the model [30]. Furthermore, the calibration degree of the model in the verification set is also checked by the same method.

Expand application

European Hypertension Practice Guidelines (2018 Edition) recommend ambulatory blood pressure monitoring for patients with grade 1 hypertension (SBP of 140-159 mmHg and/or DBP of 90-99 mmHg) or hypertensive patients without target organ damage to screen WCH [31]. Then this study took patients with grade 1 hypertension and hypertensive patients without CCVD as the subjects for ambulatory blood pressure examination according to the guidelines, and the corresponding method was called the hypertension guideline method (Method 1). Based on our scoring model, we use participants with WCH risk higher than 0.2 as screening subjects for ambulatory blood pressure monitoring, and the corresponding method is considered as the scoring model method (Method 2). We further compared the difference between the sample participation rate and WCH missed diagnosis rate between the two methods. The formula for calculating the participation rate and missed diagnosis rate is as follows.

Results

A total of 826 adults with elevated office blood pressure volunteered to participate in this study. 241 participants who took antihypertensive drugs and 32 participants who had renal insufficiency (Scr ≥ 133 mol/L) were excluded. Finally, 553 adults were included in the study, 304 males and 249 females, with an average age of 63.6 years.

Training Set and verification Set

Participants are randomly divided into the training sets and verification sets. There were 445 participants in the training set and 108 participants in the verification set. The prevalence rate of WCH in the training set was 35.1%, and that in the verification set was 44.4%. No statistical difference was found in the prevalence rate of WCH between data sets (P=0.070, Table 1). Only gender and uric acid were statistically different between the training set and the verification set (P=0.043, P=0.001, Table 1), and other modeling parameters were not statistically different between groups.

In the training set, the prevalence of ISH in WCH patients was significantly higher than that in SHT patients (P< 0.001, Table 2). SBP, DBP and TG levels in SHT patients were significantly higher than those in the WCH group (P=0. 005, P < 0.001, P=0. 021, Table 2), and the prevalence rate of CCVD in SHT patients was significantly higher than that in WCH patients (P=0.037, Table 2).

In the verification set, the prevalence rate of ISH in WCH patients was significantly higher than that in SHT patients, and SBP and DBP was significantly lower than that in SHT patients (P=0.031, P=0.001, P=0.010, Table 2). Besides, the proportion of females in WCH patients was significantly higher than that in SHT patients (P=0.016, Table 2).

Variable screening

In LASSO regression screening, the corresponding screening variables were ISH, SBP, DBP, TG, Scr, and CCVD (Figure 1). Univariate logistic regression analysis in the training set showed that the above six parameters had statistical differences between WCH patients and SHT patients (P < 0.05, Table 3), which

should be included in the next multivariate regression modeling. The area under ROC curve (AUC) of ISH, SBP, DBP, TG, Scr and CCVD were 0.608, 0.581, 0.652, 0.566, 0.555 and 0.549 respectively (Table 3).

Model construction and nomogram drawing

Multivariate logistic regression was used to construct the scoring model and draw the nomogram. In clinical application, ISH and other variables can be scored one by one, and the total score can be calculated after addition. The possibility of WCH in patients with elevated office blood pressure can be known by comparing with the nomogram (Figure 2).

Discrimination degree and calibration degree

The discrimination degree of the scoring model had statistical significance in both the training set and the verification set (P<0.001, P<0.001, Table 4). The R^2 and AUC of the scoring model in the training set were 0.163 and 0.705 (95% CI: 0.656-0.754), respectively. In the verification set, the R^2 of the scoring model was 0.206, and AUC was 0.718 (95% CI: 0.621-0.814). The model had a certain discrimination degree in both the training set and the verification set, and the discrimination degree in the training set and the verification set was close.

The calibration test results showed that the scoring model had good stability in both training set and verification set (MSE=0. 001, MAE=0. 014，MSE=0. 001, MAE=0. 025, respectively, Table 4, Figure 3).

Participation rate and missed diagnosis rate of hypertension guideline method and scoring model method

According to the practice guide method for hypertension, 499 of 553 patients with elevated office blood pressure needed ambulatory blood pressure monitoring, with a participation rate of 90.2%. 427 patients needed ambulatory blood pressure monitoring if the scoring model method was used. The participation rate was 77.2%. There was a statistical difference in the participation rate between the two methods (P 0.001, Table 5). However, the missed diagnosis rate of WCH caused by the hypertension practice guide method was 6.8%, and that of the scoring model method was 7.8%. There was no statistical difference in the missed diagnosis rate (P=0.433, Table 5).

Discussion

How to identify WCH high-risk patients during initial diagnosis is currently a clinical problem. At present, some clinicians empirically distinguish WCH from SHT by combining WCH with the clinical characteristics of the high incidence of ISH, insignificant damage to target organs, and SHT with high incidence in men and smokers and close relationship with blood lipid and kidney function [14, 32]. However, it is impossible to judge the risk of WCH scientifically and quantitatively. At present, there is still a lack of a scientific scoring model for differential diagnosis of WCH and SHT. In this study, we constructed this scoring model for differential diagnosis of WCH and SHT.

In this modeling process, LASSO regression analysis is first selected to screen research variables. LASSO regression is a relatively accurate model variable screening method at present. Compared with other variable screening methods such as ridge regression, LASSO regression can not only screen variables but also adjust complexity, effectively avoiding model overfitting [33]. In this study, 17 research variables such as gender and age were included into the LASSO regression model. Including general information such as sex and age, office blood pressure, and biochemical test results such as blood lipid and renal function, the candidate variables are all clinically readily available indicators. According to the clinical characteristics of WCH, which is high incidence in ISH patients, ISH is divided according to the characteristics of office blood pressure and included in the election variables. Blood glucose-related variables are included in DM instead of fasting blood glucose, while blood lipid variables are included in TC, TG, HDL-C, and LDL-C test results instead of hyperlipidemia. The main consideration is that blood lipid variables are more complex and have different representative meanings, so they are listed separately. Scr and UA are the most common but clinically significant renal function indicators, which are also included in the variables to be screened.

A total of six variables participating in the model construction were screened by LASSO regression, namely ISH, SBP, DBP, TG, Scr, and CCVD. These six items reflect the clinical characteristics of individual blood pressure, blood lipid, renal function, and target organ injury. For a long time, ISH has believed that it is closely related to WCH. In 2019, Feitosa et al. confirmed once again that WCH has the clinical feature of increasing ISH proportion at different age groups [14]. The results of this LASSO regression study also suggest that ISH is positively correlated with WCH. ARTEMIS research involving 27 countries around the world found that SHT is more common than WCH in patients with hyperlipidemia and renal insufficiency [34]. In this study, we also screened that TG and Scr are both positively correlated with SHT. The selected variables in blood lipid index are TG, not TC, and LDL. We speculate that the reason may be that some participants have used lipid-lowering drugs. At present, statins are the most widely used lipid-lowering drugs, and their significant reduction of TC and LDL may interfere with the research results [35]. TG is less affected by statins, so it is more suitable to be included in the scoring model.

European Hypertension Practice Guide (2018 Edition) suggests that people with grade 1 hypertension or elevated office blood pressure without obvious target organ damage should be suspected to have white coat hypertension, and further ambulatory blood pressure monitoring should be conducted to make a definite diagnosis [31]. In other words, it is based on the blood pressure level and target organ damage to judge the possibility of white coat hypertension.

The scoring model is actually an improvement of the European Hypertension Guidelines. Finally we can not only rely on SBP and DBP (reflecting blood pressure of participants) and CCVD information but also combine other parameters. Firstly, the scoring model reflects the clinical characteristics of a high proportion of ISH in white coat hypertension, and also reflects the clinical characteristics of relatively high TG and Scr in SHT.

Finally, this study uses ISH, SBP, DBP, TG, Scr, and CCVD to build a differential diagnosis model in the training set. The results suggest that ISH, SBP, DBP, TG, Scr, and CCVD alone are used to distinguish WCH from SHT and AUC are 0.608, 0.581, 0.652, 0.566, 0.555 and 0.549 respectively, and the discrimination ability is low. However, the construction of the differential diagnosis model can improve the discrimination ability of WCH. The AUC of the model applied to the training set and the verification set are 0.705 and 0.718 respectively, which is significantly improved compared with the ability of univariate WCH identification. Moreover, the AUC values of the training set and the verification set are relatively close, which indicates that the model is relatively robust [36]. Further calibration test results show that the model has good stability in both the training set and verification set.

The clinical application of this model can transform the previous empirical method of distinguishing WCH into a scientific clinical tool that can quantitatively predict the discovery of WCH diseases. Also, the model has one important use. The European Hypertension Practice Guidelines only point out that ambulatory blood pressure monitoring should be carried out for patients with grade 1 hypertension and hypertensive patients without target organ damage to identify WCH. However, the model selected participants with WCH risk higher than 20% to monitor ambulatory blood pressure. Compared with the two methods, the differential diagnosis model can significantly reduce the number of participants and save corresponding medical expenses and time loss while maintaining a similar missed diagnosis rate.

In this study, we innovatively try to distinguish WCH from SHT by scoring model, and the established model has certain clinical value. This has two disadvantages. Firstly, The training set and verification sets are randomly divided according to our own research data. The verification method used is internal verification, and the application value of the model needs a large sample of external data for verification. In addition, this model is still limited to people with normal renal function, and people with renal insufficiency cannot apply this model, so there are some limitations in its application.

Conclusion

In a word, this study established a scoring model for differential diagnosis between WCH and SHT in people with normal renal function. The scoring model has good stability and a certain discrimination degree. It can scientifically and quantitatively evaluate the possibility of WCH at the beginning of diagnosis, which is helpful to identify WCH in clinical practice.

Abbreviations

WCH, white coat hypertension; SHT, sustained hypertension; BMI, body mass index; SBP, office systolic blood pressure; DBP, office diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Glu, fasting blood glucose; Scr, serum creatinine; UA, serum uric acid; ISH, isolated systolic hypertension; CCVD, cardiovascular and cerebrovascular diseases; LASSO regression, the least absolute shrinkage and selection operator

regression; R^2, the coefficient of determination; OR, odds ratio; ROC, receiver operating curve; AUC, areas under the ROC curve; MSE, mean square error; MAE, mean absolute error.

Declarations

Ethics approval and consent to participate

The study was reviewed and approved by the Ethics Committee of Daping Hospital of the Army Medical University and registered in the Chinese Clinical Trial Registry with the registration number ChiCTR1800015507. All participants gave informed consent to the study.

Consent for publication

Not applicable.

Availability of data and materials

In attempt to preserve the privacy of individuals, clinical data will not be shared; the data can be available from authors upon request.

Authors' contributions

Peng Cai, Yan Wang, Xukai Wang: contributed to the study design. Peng Cai, Yan Peng, YuXi Chen: performed the data collection and analyses, and drafted the paper. All authors read and approved the final manuscript.

Competing interests

The authors declare that they have no actual or potential conflicts of interest.

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May my son Domi grow up healthily.

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Disclosure of conflict of interest

The authors declare that they have no actual or potential conflicts of interest

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Tables

Table 1.
Statistical analysis of the differences of research parameters between training set and verification set.

Parameters	Training set	Validation set	*P* value
Individuals	445	108	-
WCH (%)	156 (35.1)	48 (44.4)	0.070
Female□%□	191 (42.9)	58 (53.7)	0.043
Age□y□	64.0 (18.0)	65.0 (16.0)	0.734
BMI (kg/m2)	24.2 (4.4)	23.8 (3.5)	0.061
Smoking (%)	143 (32.1)	31 (28.7)	0.491
Drinking (%)	109 (24.5)	27 (25.0)	0.913
Diabetes (%)	69 (15.5)	16 (14.8)	0858
ISH (%)	220 (49.4)	55 (50.9)	0.781
SBP	144.0 (15.0)	145.0 (12.0)	0.347
DBP	90.0 (14.0)	88.5 (15.0)	0.894
HR	78.0 (18.0)	77.5 (18.0)	0.819
TC (mmol/L)	4.24 (1.37)	4.16 (1.28)	0.435
TG (mmol/L)	1.42 (1.05)	1.27 (0.75)	0.096
HDL-C (mmol/L)	1.09 (0.35)	1.11 (0.37)	0.563
LDL-C (mmol/L)	2.71 (1.01)	2.58 (0.93)	0.490
Scr (μmol/L)	66.4 (21.1)	63.9 (22.7)	0.217
UA (μmol/L)	337.2 (121.6)	303.5 (98.9)	0.001
CCVD (%)	154 (34.6)	46 (42.6)	0.121

WCH, white coat hypertension; BMI, body mass index; SBP, office systolic blood pressure; DBP, office diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Glu, fasting blood glucose; Scr, serum creatinine; UA, serum uric acid; ISH, isolated systolic hypertension; CCVD, cardiovascular and cerebrovascular diseases.

Table 2.
Statistical analysis of the differences of research variables between WCH patients and SHT patients.

Parameters	Training set		*P* value*	Validation set		*P* value#
	WCH	SHT		WCH	SHT	
Individuals	156	289	-	48	60	-
Female□%□	70 (44.9)	121 (41.9)	0.541	32 (66.7)	26 (43.3)	0.016
Age□y□	64.0 (14.0)	64.0 (18.0)	0.716	65.0 (17.0)	64.5 (15.0)	0.805
BMI (kg/m^2)	24.5 (4.5)	24.2 (4.4)	0.471	23.6 (3.8)	23.9 (3.5)	0.257
Smoking (%)	42 (26.9)	101 (22.7)	0.084	11 (22.9)	20 (33.3)	0.234
Drinking (%)	41 (24.5)	68 (23.5)	0.519	7 (14.6)	20 (33.3)	0.025
Diabetes (%)	21 (13.5)	48 (16.6)	0.381	6 (12.5)	10 (16.7)	0.545
ISH (%)	99 (63.5)	121 (41.9)	< 0.001	30 (62.5)	25 (41.7)	0.031
SBP	142.5 (14.0)	145.0 (17.0)	0.005	142.5 (7.0)	148.0 (18.0)	0.001
DBP	83.0 (13.0)	90.0 (12.0)	< 0.001	84.5 (13.0)	91.0 (17.0)	0.010
HR	78.0 (20.0)	79.0 (15.0)	0.398	76.0 (18.0)	78.0 (18.0)	0.204
TC (mmol/L)	4.23 (1.28)	4.29 (1.43)	0.277	4.16 (1.50)	4.18 (1.11)	0.936
TG (mmol/L)	1.52 (1.20)	1.34 (0.83)	0.021	1.26 (0.94)	1.27 (0.74)	0.483
HDL-C (mmol/L)	1.12 (0.35)	1.08 (0.35)	0.272	1.14 (0.38)	1.09 (0.35)	0.483
LDL-C (mmol/L)	2.70 (0.92)	2.75 (1.07)	0.293	2.59 (0.92)	2.59 (1.02)	0.850
Scr (μmol/L)	64.6 (19.3)	67.1 (21.2)	0.053	59.6 (20.0)	67.3 (23.2)	0.187
UA (μmol/L)	328.7 (112.6)	346.8 (124.9)	0.050	297.6 (87.4)	313.1 (109.3)	0.130
CCVD (%)	44 (28.2)	110 (38.1)	0.037	16 (33.3)	30 (50.0)	0.082

WCH, white coat hypertension; SHT, sustained hypertension; BMI, body mass index; SBP, office systolic blood pressure; DBP, office diastolic blood pressure; TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; Glu, fasting blood glucose; Scr, serum creatinine; UA, serum uric acid; ISH, isolated systolic hypertension; CCVD, cardiovascular and cerebrovascular disease.

Table 3.
Univariate logistic regression analysis of the research variables participating in the model construction and the results of each discrimination test.

Parameters	Univariate logistic regression		AUC (95% CI)
	OR (95%CI)	*P* value	
ISH	2.411 (1.615-3.601)	<0.001	0.608 (0.553-0.663)
SBP	0.977 (0.964-0.992)	0.002	0.581(0.526-0.635)
DBP	0.957 (0.939-0.974)	<0.001	0.652 (0.599-0.704)
TG	0.811 (0.687-0.957)	0.013	0.566 (0.512-0.621)
Scr	0.987 (0.975-0.999)	0.029	0.555 (0.500-0.611)
CCVD	0.639 (0.419-0.975)	0.038	0.549 (0.494-0.605)

SBP, office systolic blood pressure; DBP, office diastolic blood pressure; TG, triglyceride; Scr, serum creatinine; ISH, isolated systolic hypertension; CCVD, cardiovascular and cerebrovascular diseases; AUC, areas under the ROC curve; OR, odds ratio.

Table 4.
Univariate logistic regression analysis of the research variables participating in the model construction and the results of each discrimination test.

Data sets	Samples	R^2	AUC (95%CI)	*P* value	MSE	MAE
Training set	445	0.163	0.705 (0.656-0.754)	<0.001	<0.001	0.014
Validation set	108	0.206	0.718 (0.621-0.814)	<0.001	0.001	0.025

R^2, the coefficient of determination; AUC, areas under the ROC curve; MSE, mean square error; MAE, mean absolute error.

Table 5.
The difference between the participation rate of ambulatory blood pressure monitoring in outpatients with hypertension and the missed diagnosis rate of WCH patients between the hypertension practice guideline method and the scoring model method.

Methods	Total individuals (%)	Checked Individuals (%)	*P* value*	Total WCH patients (%)	Missed WCH patients (%)	*P* value#
Method 1	553 (100)	499 (90.2)	< 0.001	204 (100)	12 (6.8)	0.433
Method 2	533 (100)	427 (77.2)		204 (100)	16 (7.8)	

P value* represents the statistical difference between groups in participation rate; *P* value # represented the statistical difference of missed diagnosis rate between the groups. WCH, white coat hypertension.

Figures

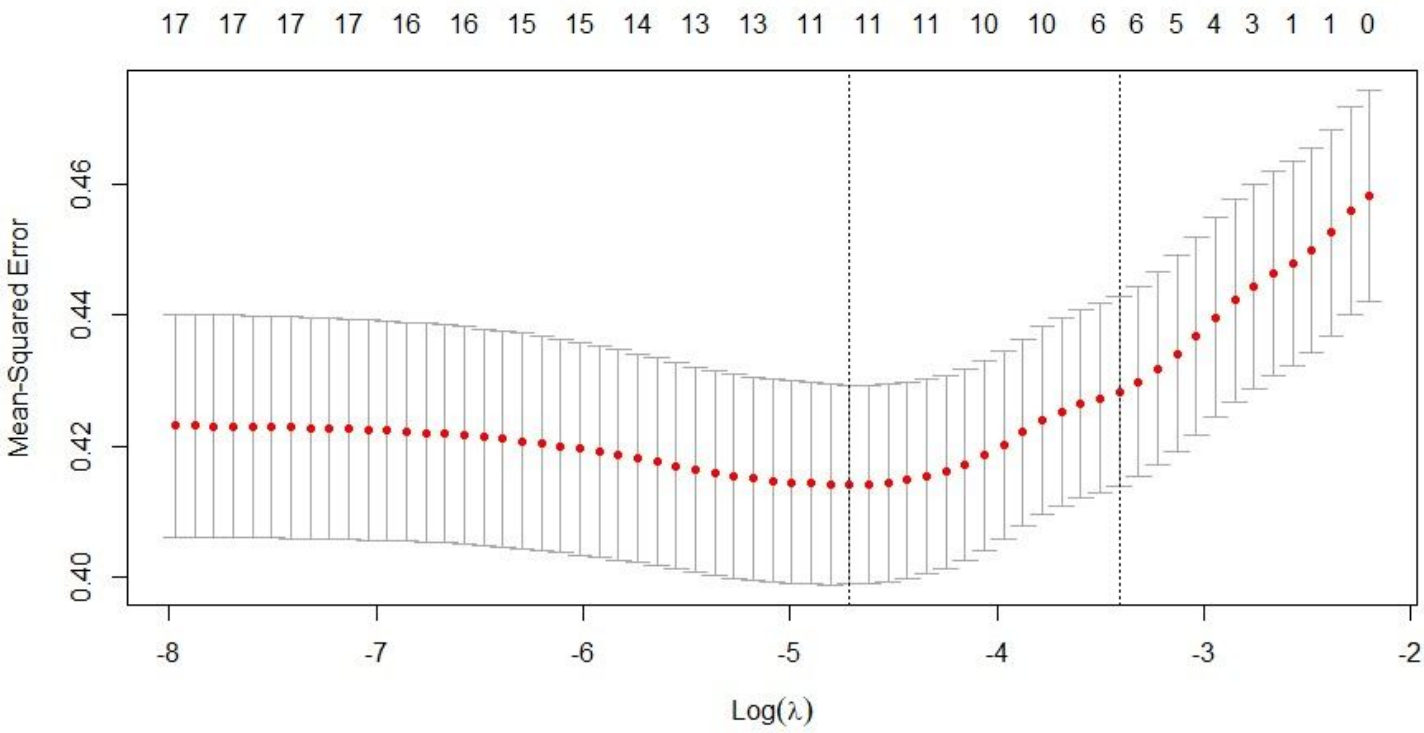

Figure 1

The result of LASSO regression analysis of variable screening in training set. LASSO regression was used to screen the research variables by 10-fold cross-validation. The upper abscissa indicated the number of selected variables, while the left vertical dotted line indicates that 11 variables were selected when the minimum penalty parameter standard was adopted, while the right vertical dotted line indicates that the number of selected variables was 6 when one standard error (1-SE standard) was adopted.

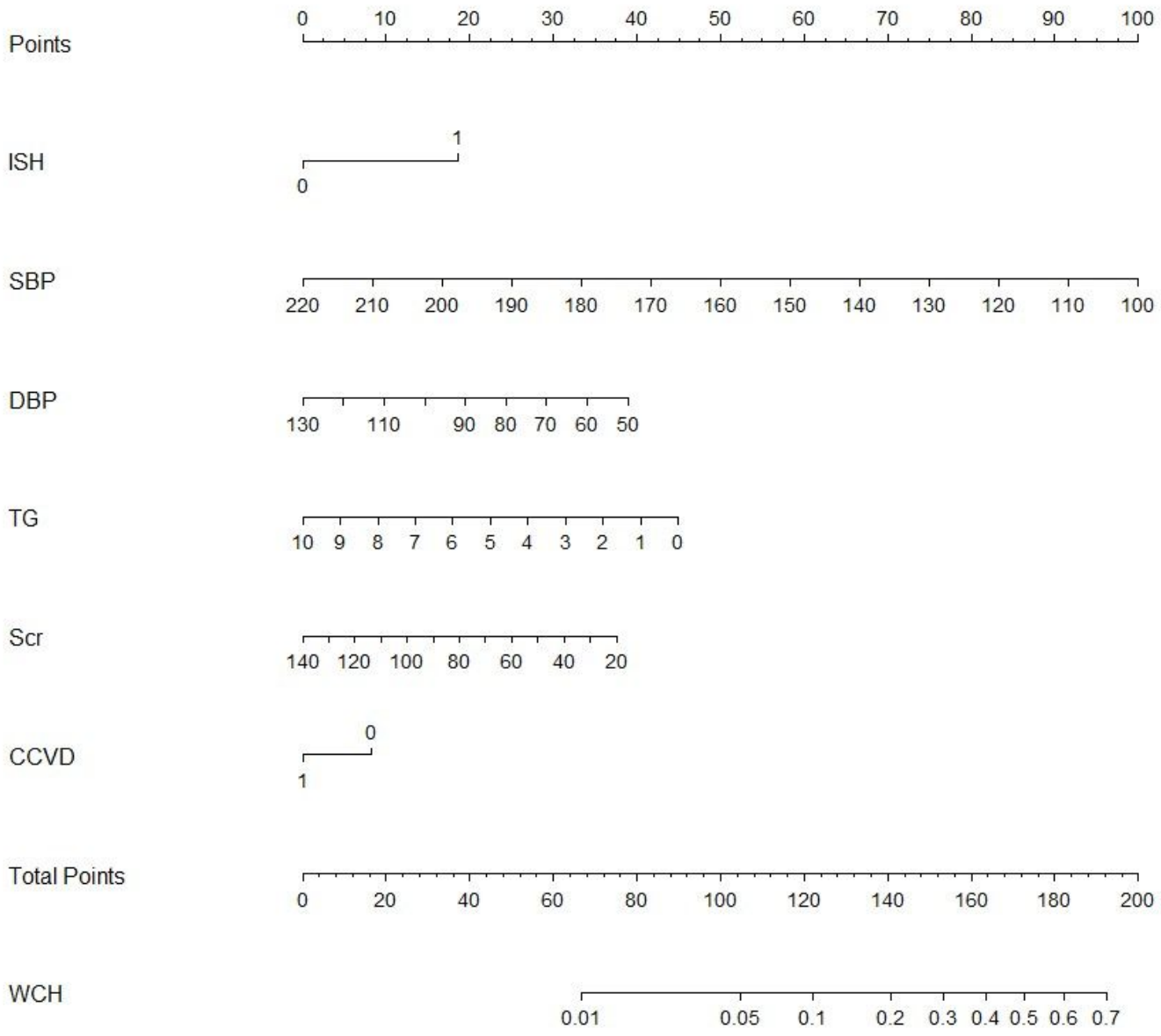

Figure 2

The nomogram for differential diagnosis of WCH and SHT. Clinicians scored ISH and other parameters one by one with reference to the nomogram, and the total score could be calculated after addition. By comparing with nomogram, we could know the possibility of WCH in patients with elevated office blood pressure.

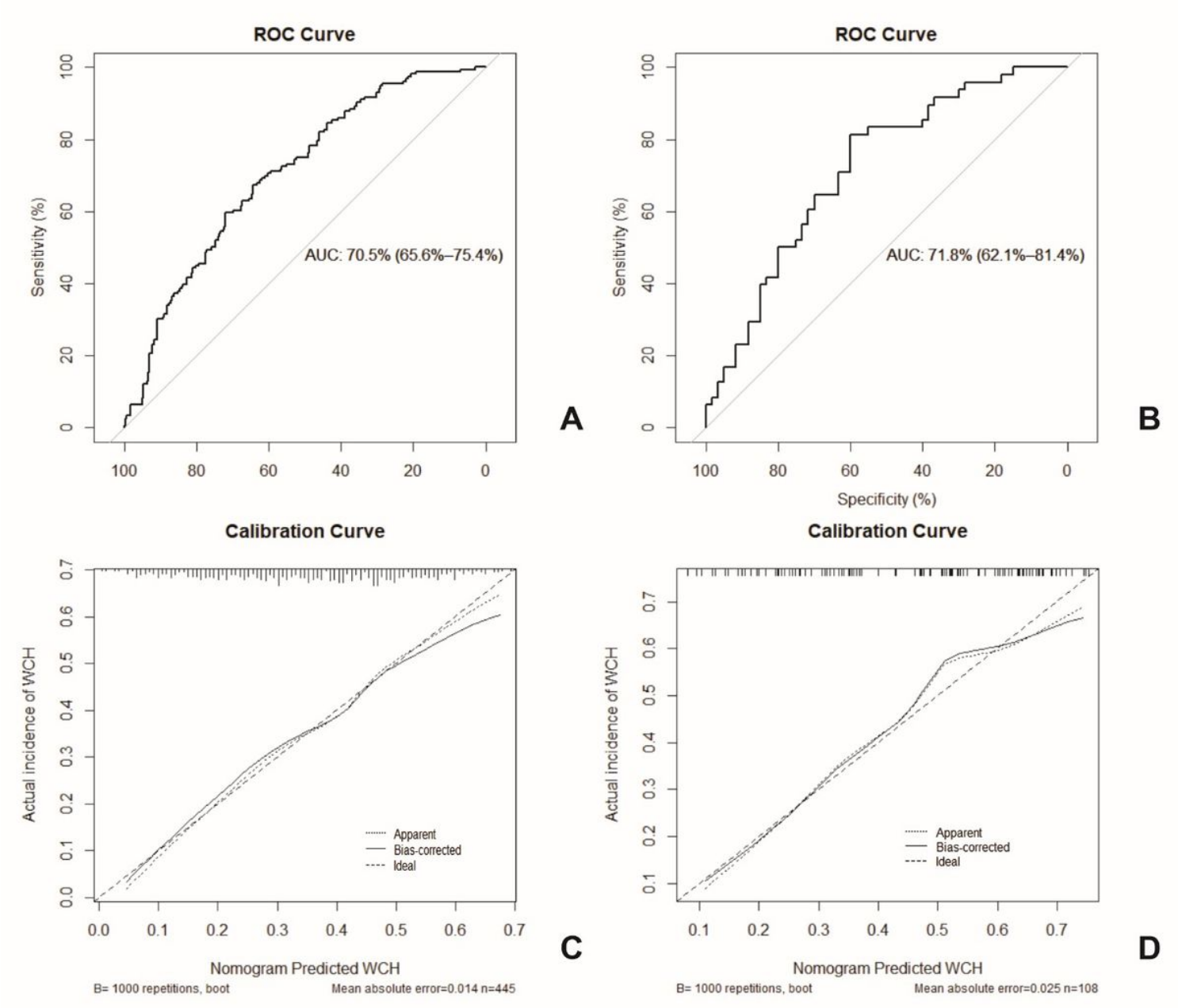

Figure 3

Discrimination and calibration test of the scoring model. Figure A and Figure B show the discrimination of the scoring model in the training set and the verification set, respectively. Figure C and Figure D suggest the calibration degree of the scoring model in the training set and the verification set respectively.

Supplementary Files

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